PATENT

In re Application of: Hauptmann et al.)	
)	
Serial No.: 09/525,998)	Before the Examiner: E. O'Hara
)	
Filed: March 15, 2000)	Group Art Unit: 1646
)	
For: TNF Receptors, TNF Binding)	
Proteins and DNAs Coding)	
For Them)	

Commissioner for Patents
Washington, D.C. 20231

Madam:

RESPONSE TO RESTRICTION REQUIREMENT MAILED MARCH 13, 2002

Responsive to the Restriction Requirement, mailed March 13, 2002, Applicants elect to prosecute those claims directed to nucleic acid molecules comprising the nucleotide sequences set forth in SEQ ID NO: 1 and SEQ ID NO: 3, designated as Group A by the Examiner, with traverse. The basis for Applicants' traversal of the requirement is as follows.

Applicants respectfully submit that there will be no undue hardship on the Office in performing a search with respect to nucleic acid molecules comprising the nucleotide sequences set forth in SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, and 19. A ClustalW multiple sequence alignment of the polypeptides encoded by these nucleotide sequences (*i.e.*, the amino acid sequences set forth in SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, and 20) is shown in Exhibit A. The sequence alignment was performed using the application MacVector 7.1.1 (Accelrys, Cambridge, UK; http://www.accelrys.com) at the default settings. This sequence alignment indicates that there is a substantial degree of homology between the amino acid sequences set forth in SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, and 20.
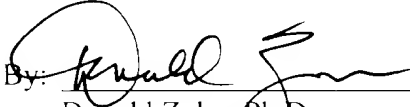
The nucleotide sequence set forth in SEQ ID NO: 1 encodes the TNF receptor protein (specification p. 3, ln. 30 to p. 4, ln. 25). The nucleotide sequence consisting of nucleotides 1

through 87 of SEQ ID NO: 1 (which is equivalent to the nucleotide sequence set forth in SEQ ID NO: 3) encodes a secretable TNF-binding protein (specification p. 4, ln. 27-41). As shown in Exhibit A, the polypeptides encoded by the nucleotide sequences set forth in SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, and 19 all possess this portion of the TNF receptor protein. Moreover, this portion constitutes between 76.3% (SEQ ID NO: 8) and 99.4% (SEQ ID NO: 6) of the polypeptides encoded by the nucleotide sequences set forth in SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, and 19. With the exception of an addition of ATG at the 5' end of the nucleotide sequences set forth in SEQ ID NOs: 5, 9, 15, and 19, the polypeptides encoded by the nucleotide sequences set forth in SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, and 19 differ only by the presence or absence of sequences encoding the signal peptide (nucleotides 1 through 87 of SEQ ID NO: 1; specification p. 21, ln. 35 to p. 22, ln. 1), the portion of pro-protein cleaved following secretion (nucleotides 88 through 120 of SEQ ID NO: 1; specification p. 22, ln. 7-11), and the linker region (nucleotides 604 through 633 of SEQ ID NO: 1; specification p. 22, ln. 12-15) of TNF receptor protein. Applicants respectfully submit that there will be no undue hardship on the Office in performing a search with respect to the nucleotide sequences of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, and 19, since a search for the elected nucleotide sequence set forth in SEQ ID NO: 3 will identify all of the non-elected sequences.

Applicants do not believe any additional fee is required. However, the Commissioner is authorized to charge any deficiency to Deposit Account No. 13-2490. If Examiner O'Hara believes it to be helpful, she is invited to contact the undersigned representative by telephone at (312) 913-0001.

<div style="text-align: right">

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

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Dated: April 3, 2002

By: Donald Zuhn, Ph.D.
Reg. No. 48,710

EXHIBIT A

ClustalW (v1.4) multiple sequence alignment

10 Sequences Aligned   Alignment Score   54899
Gaps Inserted   2   Conserved Identities   101

Pairwise Alignment Mode: Slow
Pairwise Alignment Parameters:
    Open Gap Penalty   10.0   Extend Gap Penalty   0.1
    Similarity Matrix: blosum

Multiple Alignment Parameters:
    Open Gap Penalty = 10.0   Extend Gap Penalty   0.0
    Delay Divergent = 40   Gap Distance = 8
    Similarity Matrix: blosum

Processing time: 3.9 seconds

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SEQ 2     : MGLSTVPDLLLFLVLLELNGIYPSSVIGLVPHLGDREKRNVTPQCKYI      50
SEQ 4     :                                     DSVCPQCIYI      10
SEQ 6     :                                    MDSVCPQCIYI      11
SEQ 8     : MGLSTVPELLLFLVLLELNGIYPSGVIGLVPHLGDREKRDSVCPQCFYI      50
SEQ 10    :                          MLVPHLGDREKRDSVCPQCFYI      22
SEQ 12    : MGLSTVPELLLFLVLLELNGIYPSGVIG-----------DSVCPQCFYI      39
SEQ 14    : MGLSTVPELLLFLVLLELNGIYPSGVIGLVPHLGDREKRDSVCPQCFYI      50
SEQ 16    :                          MLVPHLGDREKRDSVCPQCFYI      22
SEQ 18    : MGLSTVPELLLFLVLLELNGIYPSGVIG-----------DSVCPQCFYI      39
SEQ 20    :                                    MDSVCPQCFYI      11
                                               * * * * * * * * * *

SEQ 2     :  51 HEQNISICCTPTHKGTYLYHCPGPGQDTDCFECESGSFTASENHLFHCL     100
SEQ 4     :  11 HEQNISICCTKCHKGTYLYHCPGPGQDTDCFECESGSFTASENHLFHCL      60
SEQ 6     :  12 HEQNISICCTPCHKGTYLYHCPGPGQDTDCFECESGSFTASENHLFHCL      61
SEQ 8     :  51 HEQNISICCTKCHKGTYLYHCPGPGQDTDCFECESGSFTASENHLFHCL     100
SEQ 10    :  23 HEQNISICCTKCHKGTYLYHCPGPGQDTDCFECESGSFTASENHLFHCL      72
SEQ 12    :  40 HEQNISICCTPCHKGTYLYHCPGPGQDTDCFECESGSFTASENHLFHCL      89
SEQ 14    :  51 HEQNISICCTPCHKGTYLYHCPGPGQDTDCFECESGSFTASENHLFHCL     100
SEQ 16    :  23 HEQNISICCTPCHKGTYLYHCPGPGQDTDCFECESGSFTASENHLFHCL      72
SEQ 18    :  40 HEQNISICCTPCHKGTYLYHCPGPGQDTDCFECESGSFTASENHLFHCL      89
SEQ 20    :  12 HEQNISICCTPCHKGTYLYHCPGPGQDTDCFECESGSFTASENHLFHCL      61
                 * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

SEQ 2     : 101 SCSFCFEMGQVEISSCTVDFDTVCGCFPNDYPHYWSENLFQCFNCSLCL     150
SEQ 4     :  61 SCSFCFEMGQVEISSCTVDFDTVCGCFPNDYPHYWSENLFQCFNCSLCL     110
SEQ 6     :  62 SCSFCFEMGQVEISSCTVDFDTVCGCFPNDYPHYWSENLFQCFNCSLCL     111
SEQ 8     : 101 SCSFCFEMGQVEISSCTVDFDTVCGCFPNDYPHYWSENLFQCFNCSLCL     150
SEQ 10    :  73 SCSFCFEMGQVEISSCTVDFDTVCGCFPNDYPHYWSENLFQCFNCSLCL     122
SEQ 12    :  90 SCSFCFEMGQVEISSCTVDFDTVCGCFPNDYPHYWSENLFQCFNCSLCL     139
SEQ 14    : 101 SCSFCFEMGQVEISSCTVDFDTVCGCFPNDYPHYWSENLFQCFNCSLCL     150
SEQ 16    :  73 SCSFCFEMGQVEISSCTVDFDTVCGCFPNDYPHYWSENLFQCFNCSLCL     122
SEQ 18    :  90 SCSFCFEMGQVEISSCTVDFDTVCGCFPNDYPHYWSENLFQCFNCSLCL     139
SEQ 20    :  62 SCSHCFEMGQVEISSCTVDFDTVCGCFPNDYPHYWSENLFQCFNCSLCL     111
                 * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
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1

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SEQ  2   151  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTHLCLIQIE  200
SEQ  4   111  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTHLCLIQIE  160
SEQ  6   112  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTHLCLIQIE  161
SEQ  8   151  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTHLCLIQIE  200
SEQ 10   123  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTHLCLIQIE  172
SEQ 12   140  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTHLCLIQIE  189
SEQ 13   151  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTHLCLIQIE  200
SEQ 14   123  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTHLCLIQIE  172
SEQ 18   144  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTHLCLIQIE  189
SEQ 20   112  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTHLCLIQIE  161
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SEQ  2   201  NVFGTEDSGTIVLLILVIFFGLCLLSLLFIGLMYRYQRWKJKLYTTTTSE  250
SEQ  4   161  N                                                   161
SEQ  6   162  N                                                   162
SEQ  8   201  NVFGTEDSGTT                                         211
SEQ 10   172  NVFGTEDSGTT                                         183
SEQ 12   190  NVFGTEDSGTT                                         201
SEQ 13   201  N                                                   201
SEQ 14   173  N                                                   173
SEQ 18   190  N                                                   190
SEQ 20   161  NVFGTEDSGTT                                         172
              *

SEQ  2   251  STPEKEGELECTTTKPLAPNPSFSPTPGFTPTLGFSPVPSSTFTSSSTYT  300
SEQ  4   161                                                      161
SEQ  6   162                                                      162
SEQ  8   211                                                      211
SEQ 10   184                                                      184
SEQ 12   201                                                      201
SEQ 14   201                                                      201
SEQ 16   174                                                      174
SEQ 18   191                                                      191
SEQ 20   173                                                      173

SEQ  2   301  PGDCPNFAAPEREVAPPYQGADPILATALASDPIPNPLQKWEDSAHKPQS  350
SEQ  4   161                                                      161
SEQ  6   162                                                      162
SEQ  8   211                                                      211
SEQ 10   184                                                      184
SEQ 12   201                                                      201
SEQ 14   201                                                      201
SEQ 16   174                                                      174
SEQ 18   191                                                      190
SEQ 20   173                                                      172
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2

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SEQ 2    351  LDTDDPATLYAVVENVPFLRWKEFVRRLGLSDHEIDRLELQNGRCLREAQ  400
SEQ 4    162                                                     161
SEQ 6    163                                                     162
SEQ 8    212                                                     211
SEQ 10   184                                                     183
SEQ 12   201                                                     200
SEQ 14   202                                                     201
SEQ 16   174                                                     173
SEQ 18   191                                                     190
SEQ 20   173                                                     172


SEQ 2    401  YSMLATWRRRTPRREATLELLGRVLRDMDLLGCLELIEEAL SPAALEIA  450
SEQ 4    162                                                     161
SEQ 6    163                                                     162
SEQ 8    211                                                     211
SEQ 10   184                                                     183
SEQ 12   201                                                     200
SEQ 14   202                                                     201
SEQ 16   174                                                     173
SEQ 18   191                                                     190
SEQ 20   173                                                     172


SEQ 2    451  PSLLR  455
SEQ 4    162          161
SEQ 6    163          162
SEQ 8    212          211
SEQ 10   184          183
SEQ 12   201          200
SEQ 14   202          201
SEQ 16   174          173
SEQ 18   191          190
SEQ 20   173          172
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